

CLAIMS:

1. An isolated polypeptide comprising a portion of CFTR (cystic fibrosis transmembrane conductance regulator) protein of between 10 and 100 amino acids, said portion comprising 18 amino acids as shown in SEQ ID NO: 1.
- 5 2. The polypeptide of claim 1 which comprises 22 amino acids as shown in SEQ ID NO: 2.
3. The polypeptide of claim 1 wherein the polypeptide is fused to a membrane-penetrating peptide.
4. The polypeptide of claim 2 wherein the polypeptide is fused to a membrane-penetrating peptide.
- 10 5. The polypeptide of claim 3 wherein the membrane-penetrating peptide is selected from the group consisting of: VP-22 (SEQ ID NO: 3), (SEQ ID NO: 4), and (SEQ ID NO: 5).
6. The polypeptide of claim 4 wherein the membrane-penetrating peptide is selected from the group consisting of: VP-22 (SEQ ID NO: 3), (SEQ ID NO: 4), and (SEQ ID NO: 5).
- 15 7. The polypeptide of claim 1 which is free of phosphorylation.
8. A method of activating a CFTR protein comprising:
  - applying a polypeptide to a CFTR protein which forms a cAMP regulated chloride channel, said polypeptide comprising a portion of CFTR protein of between about 10 and 100 amino acids, said portion comprising 18 amino acids as shown in SEQ ID NO: 1, whereby the open probability of the channel formed by the CFTR increases by at least 25%.

9. The method of claim 8 wherein the open probability of the channel formed by the CFTR increases by at least 50%.
10. The method of claim 8 wherein the open probability of the channel formed by the CFTR increases by at least 75%.
- 5 11. The method of claim 8 wherein the open probability of the channel formed by the CFTR increases by at least 100%.
12. The method of claim 8 wherein the open probability of the channel formed by the CFTR increases by at least 125%.
13. The method of claim 8 wherein the open probability of the channel formed by  
10 the CFTR increases by at least 150%.
14. The method of claim 8 wherein the open probability of the channel formed by the CFTR increases by at least 200%.
15. The method of claim 8 wherein the CFTR protein is a mutant which reaches a cell's plasma membrane but fails to undergo full activation.
- 15 16. The method of claim 15 wherein the CFTR protein is listed at <http://www.genet.sickkids.on.ca/cftr-cgi-bin/fulltable>.
17. The method of claim 8 wherein the step of applying is performed by administering an aerosolized polypeptide to a patient with a mutant CFTR protein.
- 20 18. The method of claim 8 wherein the CFTR protein is in a lipid bilayer and a change in conductance is measured upon applying the polypeptide.
19. The method of claim 8 wherein the step of applying the polypeptide is accomplished by administering a nucleic acid encoding the polypeptide to a patient who expresses the CFTR protein, whereby the polypeptide is

expressed.

20. The method of claim 19 wherein the nucleic acid is administered as an aerosol to the patient's airways.
21. A method of activating a CFTR protein comprising:
  - 5 applying a polypeptide to a CFTR protein which forms a cAMP regulated chloride channel, said polypeptide comprising a portion of CFTR protein of between 10 and 100 amino acids, said portion comprising 22 amino acids as shown in SEQ ID NO: 1, whereby the open probability of the channel formed by the CFTR increases by at least 25%.
  - 10 22. The method of claim 21 wherein the open probability of the channel formed by the CFTR increases by at least 50%.
  23. The method of claim 21 wherein the open probability of the channel formed by the CFTR increases by at least 75%.
  - 15 24. The method of claim 21 wherein the open probability of the channel formed by the CFTR increases by at least 100%.
  25. The method of claim 21 wherein the open probability of the channel formed by the CFTR increases by at least 125%.
  26. The method of claim 21 wherein the open probability of the channel formed 20 by the CFTR increases by at least 150%.
  27. The method of claim 21 wherein the open probability of the channel formed by the CFTR increases by at least 200%.
  28. The method of claim 21 wherein the CFTR protein is a mutant which reaches a cell's plasma membrane but fails to undergo full activation.

29. The method of claim 28 wherein the CFTR protein is listed at  
<http://www.genet.sickkids.on.ca/cftr-cgi-bin/fulltable>.
30. The method of claim 21 wherein the step of applying is performed by  
administering an aerosolized polypeptide to a patient with a mutant CFTR  
5 protein.
31. The method of claim 21 wherein the CFTR protein is in a lipid bilayer and a  
change in conductance is measured upon applying the polypeptide.
32. The method of claim 21 wherein the step of applying the polypeptide is  
accomplished by administering a nucleic acid encoding the polypeptide to a  
10 patient who expresses the CFTR protein, whereby the polypeptide is  
expressed.
33. The method of claim 32 wherein the nucleic acid is administered as an aerosol  
to the patient's airways.
34. The method of claim 8 or 21 wherein the polypeptide is free of  
15 phosphorylation.